modulation of the AMPK/SIRT1 and TLR4/NF-κB signaling pathways. Moreover, combined therapy of CB2R agonist and AD-MSCs has a synergetic effect on cardiac repair and functional improvement after infarction.

GW26-e2179

Genetic Variation in INSIG2 was associated with Coronary Artery Disease in Uygur population in Xinjiang, China

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OBJECTIVES Dyslipidemia is a major and independent risk factor for the development of Coronary artery disease (CAD). The protein which is encoded by insulin induced gene2 (INSIG2) plays an important rules in the mediation of the feedback control of cholesterol synthesis, lipogenesis and glucose homeostasis. However, the relationship between INSIG2 genetic polymorphisms and CAD among diverse ethnicities remains unclear. The aim of the present study was to assess the association between the human INSIG2 gene and CAD in Han and Uygur population of Xinjiang, China.

METHODS A total of 681 CAD patients (334 Han, 347 Uygur) and 770 controls (346 Han, 424 Uygur) were selected for the present Case-control study. Three tagging SNPs (rs17047757, rs2161829 and rs12613329) of INSIG2 gene were genotyped using TaqMan® assays from Applied Biosystems following the manufacturer's suggestions and analyzed in an ABI 7900HT Fast Real-Time PCR System.

RESULTS In the Uygur population, for total, men and women the rs17047757 was associated with CAD by analyses of a recessive model (all, $p < 0.001$) and additive model (all, $p < 0.001$),and the difference remained significant after multivariate adjustment in a recessive model ($p < 0.001$, $p = 0.033$ and $p = 0.002$, respectively) and additive model ($p < 0.001$, $p < 0.001$ and $p = 0.035$, respectively). this relationship was also observed in rs2161829 for women by analyses of a recessive model (all, $p < 0.001$) and additive model (all, $p = 0.033$), and the difference remained significant after multivariate adjustment in a recessive model ($p < 0.001$, respectively). However, this relationship was not observed in this three tagging SNPs before and after multivariate adjustment in Han population.

CONCLUSIONS Our results indicated that both rs17047757 and rs2161829 in the INSIG2 gene was associated with CAD in Uygur population in Xinjiang, China.

GW26-e2408

Left renal sympathetic stimulation and ablation affect ventricular arrhythmia by modulating left stellate ganglion in a cesium-induced long QT canine model

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OBJECTIVES Our previous study has shown that left renal sympathetic stimulation (LRS) may facilitate ischemic ventricular arrhythmia (VA) by increasing neural activity of left stellate ganglion (LSG). Furthermore, studies have shown that renal sympathetic ablation (LRA) may be anti-arrhythmia. Therefore, we hypothesized that renal sympathetic intervention may affect VA by modulating LSG activity in a cesium induced long QT canine model.

METHODS Twenty-four dogs were randomly divided into three groups, group 1 (n=8,LRS), group 2 (n=8, LRA), group 3 (n=8, LRS followed LSG ablation). Ventricular effective refractory period (ERP), heart rate variability (HRV), serum norepinephrine, BP elevation in response to LSG stimulation and LSG activity were measured before and after autonomic intervention. Following, dose injection of cesium was conducted and then early afterdepolarization amplitude, VA prevalence and tachycardia threshold as measured by dose of CsCl were compared among these groups.

RESULTS In group 1, 3-hour LRS significantly decreased ventricular ERP at all sites and HRV, increased serum norepinephrine and LSG neural activity, and augmented BP elevation in response to LSG stimulation as compared to group baseline. In group 2, however, LRA resulted in a reverse result. Furthermore, no significant change was shown in ventricular ERP, HRV, serum norepinephrine, BP elevation in response to LSG stimulation or LSG neural activity in group 3. As compared to group 1, the early afterdepolarization amplitude and VA prevalence were significantly reduced, and the tachycardia threshold was significantly higher in group 2 and group 3.

CONCLUSIONS LRS and LRA might facilitate and prevent VA, respectively, by modulating LSG neural activity in cesium-induced long QT canine model.

GW26-e2420

Danhong Injection Prevents Nitroglycerin-induced Tolerance in Rat

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OBJECTIVES Danhong Injection (DHI) is a traditional Chinese medicine consisted by two herbal medicines, Radix et Rhizoma Salviae Miltiorrhizae and Rhizoma Flos Carthami, which is used in clinic as a remedy for cardiovascular diseases. The early studies indicated that DHI has protective effect on endothelial cells. This study aimed to investigate the potential effects of DHI on nitroglycerin-induced tolerance in rats.

METHODS Nitroglycerin-induced tolerance was induced by pretreatment with nitroglycein (50 mg/kg) once a day for three days on Wistar rats. DHI was co-treated in this period. In addition, the maximal relaxation response curve was drawn and malondialdehyde (MDA) level, nitric oxide synthase (NOS) activity and cyclic guanosine monophosphate (cGMP) level were measured. In vitro, the tolerance was induced by exposure the isolated thoracic aorta obtained from rats to nitroglycerin (10^{-4} M) for 60 min with pretreated of DHI. In addition, nitric oxide synthase inhibitor (L-NAME), ornithine cyclase inhibitor (ODQ) and cyclooxygenase inhibitors (Indo) were used to study the mechanism.

RESULTS DHI could significantly reduce the MDA content ($P < 0.05$), increase NO and cGMP ($P < 0.05$) in comparison with nitroglycerin-induced tolerance. Pre-exposure of aortic rings to nitroglycerin significantly reduced the relaxation to nitroglycerin ($P < 0.05$) in comparison with controls. Treatment with DHI could increase relaxation's response compare with nitroglycerin-induced tolerant aortic rings ($P < 0.05$).

CONCLUSIONS DHI significantly attenuates nitroglycerin-induced tolerance in vivo and in vitro. The mechanism is at least partly based on endothelium protection and anti-oxidant.

GW26-e4536

The study of asiatic acid effects on isoprenaline induced cardiac hypertrophy

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OBJECTIVES To study whether asiatic acid (AA) attenuate cardiac hypertrophy through the mitogen-activated protein kinase (MAPK) and phosphoinositide 3-kinase (PI3K) signaling.

METHODS Cardiac hypertrophy in mice was induced by subcutaneous administration of isoproterenol. 30 mice were divided into three groups (10 mice per group): Sham (saline), ISO (saline) and ISO+AA. The mice were subcutaneously given a dose of 50mg/kg of AA 2 times a day for two weeks, meanwhile mice in the Sham and ISO group received the same volume of normal saline. The heart weight (HW), tibia length (TL) and body weight (BW) were recorded and then calculated the ratios of HW/BW and HW/TL. Sections of heart were stained with hematoxylin and eosin for histopathology or picrosirius red for collagen deposition. The cross-sectional areas (CSA) of the myocytes was also counted. The signaling pathway involved in the cardiac hypertrophy was also detected by western blot.

RESULTS Compared to the ISO group, the HW/BW, HW/TL, CSA were obviously reduced in the ISO+AA group. In addition, the parameters of cardiac fibrosis were obviously improved. Meanwhile, the expressions of phospho-Akt, phospho-Gsk3β, phospho-Erk, phospho-P38 were markedly reduced.

CONCLUSIONS Our data suggest that AA can attenuate cardiac hypertrophy through blocking the MAPK and PI3Ksignaling.

GW26-e4771

Protective and antiapoptotic effects of luteolin on oxidative injury in H9C2 cardiomyocytes

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OBJECTIVES Luteolin, a falconoid compound in many types of plants, plays important cardioprotective roles in cardiovascular

diseases. But its underlying mechanism needs to be furtherelaborated. The purpuse of this study was to identify the protective and antiapoptotic effects of luteolin on oxidative injury in H9C2 cardiomyocytes and to clarify the underlying mechanism.

METHODS A model of hydrogen peroxide (H_2O_2)-induced H9C2 cells oxidative injury was established in vitro. The changes in cell viability were examined with an MTT assay to determine the available concentration of H_2O_2 and luteolin. 2', 7'-Dichloroflurescin diacetate (DCFH-DA) and flow lytometry were used to detect the effect of luteolin on ROS level and apoptosis degree respectively. We also used Real time fluorescent quantitative PCR to examine the effect of luteolin on the regulation of caspase-3, bcl-2, bax and the ratio of the latter two.

RESULTS We found that incubation with various concentrations of H_2O_2 (0,25,50,100,200) for 1h caused dose-dependent loss of cell viability and 100μM H_2O_2 approximately reduced the cell viability to 50%. Treatment with 10μM luteolin effectively decreased the level of H_2O_2-induced injury. Result of DCFH-DA indicated that 100μM H_2O_2 also increased the ROS level in H9C2 cells, while luteolin obviously reversed this increase. Moreover, the flow cytometry result suggested that luteolin could effectively inhibit apoptosis induced by H_2O_2 in H9C2 cells. PCR results further verified that luteolin downregulated the expression of caspase-3 caused by H_2O_2, and upregulated the ratio of bcl-2 and bax.

CONCLUSIONS Luteolin protects H9C2 cells from H_2O_2-induced oxidative injury by reducing intracellular ROS level and decreasing apoptosis. The protective and antiapoptotic effects of luteolin may be related to its regulation on decreasing caspase-3 and increasing the ratio of bcl-2 and bax.

GW26-e0461

Exosomes secreted from dendritic cells induce angiogenesis by cardiac microvascular endothelial cells after myocardial infarction

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OBJECTIVES It has been reported that the infiltration of dendritic cells (DCs) significantly increased in infarcted myocardium after myocardial infarction (MI) and DCs ablation impaired angiogenesis post-MI in mice. However, the mechanism of how DCs exert effects on MI is still not completely understood. Exosome (EX) has been known as the messenger between cells, this study was aimed to clarify whether EXs derived from DCs induce angiogenesis by cardiac microvascular endothelial cells via paracrine signaling post-MI.

METHODS DCs were derived from mouse bone marrow-derived DCs (BMDCs) and primary cultured rat cardiac microvascular endothelial cells (CMECs) were used to form vasculatures. BMDCs suspensions were incubated with the supernatant of necrotic or normal cultured HL-1 myocardial cells for 24 hrs respectively (as necrosis or control group). EXs were then isolated from the supernatant of BMDCs (DC-Exosomes, DEXs) and identified by electron micrograph and Western blotting using the exosomal marker. DEXs were added to CMECs and the angiogenesis was evaluated by measuring the tube formation and VEGF expression. Finally, the expression profiling of miRNA in splenic DCs of MI mice was analyzed by Affymetrix miRNA 4.0 chip assays and the significantly up-expressed and highly enriched miRNAs were certified both in DCs and DEXs by quantitative RT-PCR.

RESULTS Confocal imaging showed DEXs could be uptake by CMECs. Compared to the control group DEXs, DEXs from necrosis group significantly up-regulated the expression of VEGF in CMECs and enhanced the tube formation by CMECs. Some miRNAs including miR-16-5p, 23a-3p, 150-5p, and 126-3p which are associated with angiogenesis were significantly up-regulated and highly enriched in DEXs from necrosis group compared to those from control group.

CONCLUSIONS These results suggest that exosomal miRNAs especially angiogenetic miRNAs could be secreted from DCs and promote angiogenesis by CMECs post-MI. Our study may present a potent and novel DEXs-based therapeutic approach for MI treatment.

GW26-e0470

miR-124 regulation of NFATC1 and atherosclerosis in apolipoprotein E-deficient mice

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OBJECTIVES Atherosclerosis, a chronic inflammatory disease, is the leading cause of death and disability worldwide. Evidence supports a role for microRNAs (miRNAs) in cardiovascular pathophysiology and atherosclerosis development. Herein, we explore the effects of miR-124 on atherosclerosis in apolipoprotein E(-/-) (ApoE-/-) mice.

METHODS A constrictive collar was placed around the right carotid arteries of that were fed a high-fat diet to induce atherosclerotic plaque formation, miR124a-expressing lentiviral vectors (LV) in the presence or absence of recombinant LVTHM-NFATC1 or pGC-FU-NFATC1 was transfected into right carotid plaques respectively.

RESULTS Up to 3-fold downregulation of miR-124 and about 2-fold enrichment of NFATC1 were detected in the models. Consistently, miR-124-expressing resulted in decreased aortic atherosclerosis, impaired pro-inflammatory burden, as evidenced by reduced blood monocytes, endothelial inactivation- and inflammatory markers in aorta, and pro-inflammatory cytokines, chemokines in plasma of ApoE-/- mice compared with the control group. Not surprisingly, silencing NFATC1 mimicked these effects. However, restoration of NFATC1 effectively and consistently attenuated the atherosclerotic suppression phenotypes elicited by the miR-124. Further analysis identified NFATC1 as a direct target of miR-124.

CONCLUSIONS Taken together, the current results reveal, for the first time, a potential molecular regulation of miR124 on NFATC1, offering a possible therapeutic approach for atherosclerosis.

GW26-e0479

Changes of plasma angiotensin II and aldosterone in rat model of salt-sensitive hypertensive induced by sensory denervation

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OBJECTIVES Observe the changes of hypertension and plasma angiotensin II and aldosterone in rat model of salt—sensitive hypertensive induced by sensory denervation and to realize the relationship between the hypertension and the angiotensin 11 and aldosterone, therefore explore the mechanism of the hypertension.

METHODS New—born Wistar rats were injected capsaicin(50 mg / kg) hypodermically and the control rats were injected vehicle. After lactation male rats were chosen, divided into four groups and fed the diets with different salt contents respectively for 16 weeks. The tail systolic pressure, plasma concentrations of angiotensin IIand aldosterone in 4W,8W,12W,16w were detected.

RESULTS The control group and the model group's hypertension in 4w 8w 12w 16w were (107±5.9vs141±3.9), (110±4.7vs153±5.2), (111±4.2vs163±4.2), (105±5.5vs177±5.0)mmHg($P>0.05$), The control group and the model group's angiotensin in 4w 8w 12w 16w were 541±12.1vs 250±11.3), (522±10.3vs 318±12.4), (545±11.4 vs 399±17.6), (532±17.1vs 477±15.7)ng/L($P>0.05$), The control group and the model group's aldosterone in 4w 8w 12w 16w were(642±24.1vs256±22.4), (625±23.3vs342±20.6), (645±31.4vs443±28.8), (629±22.7vs490±19.1)ng/L($P>0.05$).

The blood pressure of CON+NS group have no difference with the CAP+NS group. The blood pressure of CAP+HS group in 4 week was higher than other groups($P<0.05$), rising from 4 week to 16 week. Salt loading reduced angiotensin II as well as the aldosterone concentrations in plasma of rats. Compared with control group, the CON+HS group in 4 week have no difference, rising from 8 week. The angiotensin IIand the aldosterone of the CAP+NS group have no difference with the control group, the CON+HS group was lower than control group. CON+HS group rise from 8 week to 12 week.

CONCLUSIONS The establishment of rat model of salt—sensitive hypertensive induced by sensory denervation may be related to renin-angiotensin··aldosterone system.